Medical Information

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Syncope and Transient Loss of Consciousness

Differential Diagnosis and Treatment

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TRANSIENT LOSS of consciousness is a common complaint in any emergency room or physician's office. In most cases the cause of such events is rapidly established, simple faints and epilepsy making up the majority of diagnoses. The challenge then is not to overlook the relatively less common and often less benign causes.

The differential diagnosis is presented here.

Simple Faints

Vasovagal disorders are exceedingly common and occur in all age groups (mean age is 40 years old). Males and females are affected equally. Common causes include emotional stimulation, injury, pain, sight of blood, sudden exposure to cold, fatigue, instrumentation and blood loss (for example, 5 percent of blood donors giving 500 ml experience syncope; 50 percent of patients donating 1,000 ml experience syncope).[1]

Vasovagal episodes begin in a standing or sitting position, never in a horizontal position. The prodrome lasts from between 10 and 20 seconds to a few minutes and can include weakness, lightheadedness, nausea, pallor, diaphoresis, salivation, blurred vision and tachycardia. Subsequently, the patient falls to the ground, pale and diaphoretic, with mydriatic pupils and slow, weak pulse (tachycardia becomes bradycardia as consciousness is lost). Movements may be noted during unconsciousness. They are mainly tonic, often opisthotonic.[2] Occasionally urinary incontinence or seizure-like tonic-clonic movements are noted.[3] Tongue biting is rare. The electroencephalographic electrical activity becomes flat, clearly differentiating vasovagal episodes from seizures. Secondary cerebral hypoxia and tonic-clonic movements are more likely to occur if the patient is kept in an upright position.

The patient is alert and awake shortly after assuming a horizontal position (seconds to a few minutes). Residual nervousness, dizziness, headache, nausea and vomiting, pallor and diaphoresis are not uncommon. A desire to defecate may be noted. If the patient stands during the next thirty minutes, syncope may recur.

Physiologically, both decreased arterial tone and bradycardia combine to produce central nervous system hypoperfusion[4] although examples of pure vasodepressor (hypotension) or cardioinhibitory (bradycardia) syncope have been described.[2] Syncope without alteration in blood pressure or heart rate is termed cerebral[5] but its existence is doubtful.[2] Ocular compression[2] (oculovagal reflex) or the Valsalva maneuver[6] may be helpful in showing abnormal sensitivity to vagal stimulation and thus providing evidence of a vasovagal cause for episodes of loss of consciousness in a given patient. In one series, ocular compression produced loss of consciousness in 20 percent of patients fainting, and transient cardiac standstill in 70 percent.[2]

In view of the pathophysiology of these episodes, trials of belladonna alkaloids, ergot alkaloids or barbiturates (or combinations of these) have been recommended as therapy.[7,8]

Seizures

Seizures are an exceedingly common cause of episodic loss of consciousness, affecting 0.4 percent of the population. The history of a seizure is one of sudden onset of symptoms. An aura, if present, is brief but may have localizing significance such as olfactory, gustatory or deja-vu auras in temporal lobe seizures; focal, sensory or motor symptoms in frontoparietal lobe foci; visual scotomata in the occipital lobe. Seizures may begin in any position and 20 percent of persons with epilepsy have seizures only during sleep. Generalized tonic-clonic movements are commonly noted; however, a predominance of somatosensory symp-

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toms, tonic posturing or temporal lobe manifestations (auditory, vertiginous, visceral phenomena; psychomotor automatisms) make diagnosis more difficult. Cyanosis is frequent during seizures; pallor is uncommon; breathing is often stertorous.

In the differential diagnosis of episodic loss of consciousness the most distinctive feature of epilepsy is a period of altered consciousness (postictal state) following the seizure. This period is usually limited to a few minutes of disorientation. However, prolonged alteration of consciousness may occur during status epilepticus, and is seen postictally in patients with diffuse structural cerebral damage (for example, status post multiple cerebral infarctions, senile dementia) or following seizures resulting from acute encephalitis or hyponatremia.[9]

Findings on physical examination during the postictal state commonly will be normal or will show only positive Babinski signs. The patient frequently experiences headache. Pupils are always reactive to light, even in unresponsive patients. Lateralizing motor findings or focal motor onset may localize the central nervous system lesion. The epileptic postictal state stands in strong contrast to vasovagal episodes where consciousness and orientation are regained in close aposition. A history of urinary incontinence or of a few jerking or clonic movements is of dubious differential value since these symptoms can be found in both simple vasovagal syncope and in epilepsy.

Although idiopathic epilepsy is by far the most common cause of seizures, important additional causes include purulent meningitis, uremia, acute anoxia from any cause (such as cardiac arrest or arrhythmia), hyponatremia, hypoglycemia, hypocalcemia, hypertensive encephalopathy, rapid decrease in anticonvulsant drug levels, embolic cerebrovascular disease and head trauma. Acute withdrawal from ethanol in chronic abusers may produce seizures, 90 percent of which occur during the first 7 to 48 hours.[10] Seizures are generalized and occur in a brief flurry, most commonly one to six in number. Medical intervention is usually unnecessary since the seizures are selflimiting. Diphenylhydantoin sodium (Dilantin®) therapy is said to be ineffective acutely but this may be due to the time needed to administer a therapeutic dose.[11] There is some suggestion that barbiturates[12] or chlordiazepoxide[13] might be effective prophylactically, but patient compliance is of course a problem. Phenobarbital (200 mg given intramuscularly one time) is adequate acutely if needed. Drug withdrawal seizures are seen following withdrawal from daily doses of sodium secobarbital (Seconal®) greater than 450 mg a day or the equivalent amount of other sedative hypnotics (although seizures are more commonly seen when doses of 600 to 800 mg have been used).[14] Sedative-hypnotic drug abuse should be treated in hospital by gradual withdrawal (approximately one therapeutic dose daily).

Once a seizure disorder is suspected, supportive evidence can be gained from electroencephalography, but findings on a single tracing can be normal in more than 40 percent of patients with epilepsy.[15] Anticonvulsant therapy is dictated by the cause of the seizure and varies from brief observation (ethanol withdrawal) to chronic anticonvulsant therapy (idiopathic epilepsy). If an anticonvulsant is indicated, administration of Dilantin (1,000 mg given orally during the first 24 hours, 500 mg given orally during the second 24 hours and 300 mg given orally each day thereafter) is a common first-line approach while diagnostic studies are being made. This regimen will provide therapeutic blood levels in 24 hours; 1 gram given intravenously (50 mg per minute) will produce a rapid therapeutic response. Nystagmus on lateral gaze is correlated with Dilantin levels above 2 mg per 100 ml and is therefore a helpful indicator of adequate anticonvulsant therapy (minimum therapeutic levels are 1 to 2 mg per 100 ml).[16]

Cardiovascular Syncope

Syncope in the recumbent posture is very suggestive of a cardiac-related cause. It may occur secondary to sinus arrest, bradyarrhythmia (with rate below 30) or tachyarrhythmia. Acute myocardial infarction is an important exclusion; in one series, loss of consciousness was reported in ten of 200 such patients.[17]

Stokes-Adams

Syncope due to transient bradyarrhythmias and asystole has been termed the Stokes-Adams syndrome.[18] Episodes are as common in men as in women and occur mainly in the sixth or seventh decade. There is often no prodrome. Onset is rapid with loss of consciousness in 3 to 5 seconds —or within 15 seconds if the patient is recumbent. Convulsion and fecal incontinence are not uncommonly seen as duration of cerebral hypoperfusion becomes greater. Recovery of consciousness

is rapid, within seconds to a few minutes. A postictal confusional state is expected in patients who convulse; otherwise, no residual is seen.

Findings on electrocardiograms made following Stokes-Adams attacks can be normal, especially after sinus arrest or third degree atrioventricular block.[19] Several syndromes of episodic loss of consciousness with prolonged Q-T interval have been described;[20] such as congenital deafness, syncope, prolonged Q-T interval and sudden death secondary to ventricular fibrillation.[21] Tape recorded continuous portable electrocardiograph monitoring and measurement of cardiac enzymes are essential aspects of the evaluation.

Tachyarrhythmias

Tachyarrhythmias with heart rates greater than 180 to 200 beats per minute produce syncope in approximately 50 percent of patients, depending on age.[22] Periods of asystole sufficient to produce syncope have been observed following the cessation of a supraventricular tachycardia[23] (the sick sinus syndrome). While digitalis may be the drug of first choice for prophylaxis in some supraventricular arrhythmias, a pacemaker may be required for the sick sinus syndrome.[24]

Aortic Stenosis

Loss of consciousness secondary to aortic stenosis has been observed in all age groups. Episodes are especially common following exercise and are often associated with dyspnea, angina and diaphoresis. Two phases are recognized: acute left ventricular failure with normal sinus rhythm lasting 40 seconds, and a second stage of ventricular arrhythmia or cardiac standstill producing apnea, cyanosis and convulsion. Sudden death may result.[25]

On examination, there is a carotid pulse with slow upstroke and low peak (pulsus parvu et tardus) in most patients with hemodynamically-significant aortic stenosis, but this sign may be absent. A systolic thrill is perhaps better correlated with aortic valve pathology (in combination with the characteristic murmur). Failure to find evidence on x-ray studies of aortic valve calcification in patients over 35 makes diagnosis of aortic stenosis highly suspect.[26] Symptomatic aortic stenosis (angina, failure, syncope) requires valve replacement since average survival following syncope is three years.[27].

IHSS (Idiopathic Hypertrophic Subaortic Stenosis)

Most commonly IHSS[28] becomes symptomatic between the second and fourth decades. Syncope, frequently associated with exercise, was noted in 30 percent of cases in one series and was the presenting symptom in 10 percent of cases (with orthostatic and post-tussive syncope also reported); dyspnea, however, was the most common presenting symptom (60 percent of all cases).

On examination, suggestive features are a double apical impulse, precordial thrill, paradoxically split second sound, third and fourth heart sounds, and a long systolic murmur with mid-systolic accentuation maximum at the lower left sternal border or apex. Syncope in IHSS may not be associated with hemodynamic evidence of left ventricular outflow obstruction. Propranolol has been the most useful therapeutic agent.

Pulmonary Hypertension

Syncope, often secondary to effort, can be associated with pulmonary hypertension and may be the presenting symptom. Signs of right ventricular failure may be found: parasystolic heave, increased pulmonic second sound (P_2), murmur of pulmonic insufficiency or electrocardiographic evidence of right ventricular hypertrophy. Pulmonary emboli are often an unrecognized cause of pulmonary hypertension and may present with only sudden loss of consciousness.[29]

Other cardiac lesions associated with loss of consciousness are tetralogy of Fallot, ball variance in valve prostheses and atrial mysoma.

Cerebral Vascular Syncope

Cerebral vascular disease is an often diagnosed but actually uncommon cause of episodic unconsciousness. Several distinct entities deserve comment.

Basilar Artery Insufficiency

Basilar artery insufficiency and basilar artery transient ischemic attacks (TIA's) occur most commonly after the sixth decade. Episodes begin almost exclusively in the sitting or standing position.[30] The symptom complex of diplopia, vertigo, dysphasia, dysarthria, various sensory or motor symptoms, drop attacks and occipital headaches suggest diffuse areas of brain stem ischemia. Episodes are of sudden onset and brief duration (seconds to minutes). Isolated episodes of unconsciousness occur only rarely. When loss of con-

sciousness is included in the symptom complex, recovery is prolonged (30 to 60 or more minutes). Transient vertebral artery occlusion secondary to nuchal compression on head turning or to cervicocranial anomalies is one treatable cause of basilar artery ischemia.[31] In general, however, the therapy for these disorders is unclear; and recurrent episodes have been observed in 68 percent of cases and strokes in 18 percent of cases in one study.[32] Anticoagulation with sodium warfarin (Coumadin®)[33] or acetylsalicylic acid (aspirin) should be employed for at least two months.[34]

Migraine

Syncope, often secondary to rapid standing, has been reported in 10 percent of 500 patients with migraine,[35] suggesting that the loss of consciousness is due to orthostatic hypotension. In the specific syndrome of basilar artery migraine,[36] the migrainous vasoconstriction involves the basilar artery and produces symptomatology similar to basilar artery transient ischemic attacks. Most cases described occur in adolescent girls; however, additional documented cases in adults support this clinical entity.[37] Medical therapy with antimigraine drugs is often effective.

Takayasu's Disease

Takayasu's disease (aortic arch syndrome, pulseless disease) is a panarteritis of the great vessels occurring nearly exclusively in girls. Prominent symptoms include those of hypoperfusion of the central nervous system—such as decreased vision and confusion. Syncope or loss of consciousness was noted in 75 percent of patients with this disease in one series, particularly following exercise, standing or head movement.[38] On physical examination, decreased or absent peripheral pulses and low recorded blood pressure in the arms are found.

Carotid Sinus Syncope

Carotid sinus syncope is a rare condition, though commonly discussed. Men are affected twice as often as women and most have passed the sixth decade of life. Classically, pressure of the carotid sinus by a tight collar, neck mass, cervical nodes or tumor causes vagal stimulation of the sinoatrial and atrioventricular nodes and a sympathetic inhibition. Bradycardia and hypotension result producing syncope; the bradycardia is blocked by administration of atropine.[39] Many cases misdiagnosed as hypersensitive carotid sinus have been found to be secondary to ipsilateral carotid compression with contralateral carotid occlusion. Diagnosis, then, demands knowledge of the patency of the cerebral circulation, or at least the presence of good carotid pulses bilaterally with loss of consciousness on carotid stimulation without manual occlusion of the vessel.[40]

Miscellaneous

Orthostatic Hypotension

Orthostatic hypotension occurs in males slightly more frequently than in females. It is most common in the sixth and seventh decades but may also appear in the teens. Drug ingestion is a major cause; a list of drugs commonly involved is given in Table 1.[41]

Loss of consciousness usually occurs as a result of rapid standing. Prolonged motionless standing (especially following exercise) and standing after prolonged bed rest (especially in elderly patients) are other frequent causes. Orthostatic syncope may be the presenting symptom of acute blood loss or Addison's disease, or may follow sympathectomy. Orthostatic changes can be associated with peripheral neuropathies—such as diabetes mellitus (orthostatic changes occur in 30 percent of patients), alcoholism, Guillain-Barre syndrome or amyloidosis. With central nervous system lesions, autonomic nervous system involvement produces orthostatic hypotension in Wernicke's encephalopathy, the myelopathy of multiple sclerosis, and tabes dorsalis. Idiopathic orthostatic hypotension when part of the Shy-Drager syndrome is characterized by anhidrosis, sphincter disturbances, parkinsonism and impotence; no postural change in pulse is seen.[42]

TABLE 1.—*Drugs Commonly Involved in Orthostatic Hypotension*

Amitriptyline	Iopanoic acid
Benzothiadiazines (Chlorothiazide, hydrochlorothiazide polythiazide)	Levodopa
	Lidocaine
	Monoamine oxidase inhibitors
Bretylium	Methotrimeprazine
Chlorisondamine	Methyldopa
Clonidine	Methysergide
Desipramine	Nitroglycerine
Furosemide	Pentolinium
Guanacline	Phenoxybenzamine
Guanethidine	Procarbazine
Guanoxan	Protriptyline
Hexamethonium	Reserpine
Imipramine	Thiothixene

Important studies include orthostatic blood pressure measurements, hematocrit, stool guaiac and—in equivocal cases—tilt-table testing.[43] Immediate therapy includes discontinuing any offending medication, gradual standing, placing head of bed on blocks and use of support stockings. Longer-term therapy is dictated by the specific cause of the hypotension. Administration of 9-alpha-fluorohydrocortisone has been effective in idiopathic cases, beginning with 0.1 mg daily with gradual increases as necessary to as much as 1.0 mg daily.[44,45]

Hyperventilation

Hyperventilation is a common cause of altered consciousness manifested by light-headedness, shortness of breath, numbness and tingling (especially circumoral) and muscular twitching. Its culmination in syncope is unusual; however, the occurrence has been described.[46] Loss of consciousness is produced by hypocapnea-induced cerebral vasoconstriction resulting in hypoxia. Women are affected much more often than men and patients are usually in the third or fourth decade. This disorder is most often benign with anxiety as a prominent precursor but cardiopulmonary causes for dyspnea must be excluded. The syndrome commonly occurs when a patient is lying down, a helpful differential diagnostic point. Tetany is rare although nearly diagnostic. Patients often claim prolonged unconsciousness; upon close questioning, however, this is rarely the case. Often, hyperventilation at the examiner's request will duplicate symptoms.

Post-tussive Syncope

Post-tussive syncope occurs primarily in elderly men with chronic obstructive pulmonary disease but has been reported in children.[47] Coughing, not necessarily prolonged, immediately precedes the attack which is notable for its possible occurrence when the patient is lying down. Prodromal symptoms of syncope are often absent, and the duration of unconsciousness is less than one minute. Recovery is immediate. A history of similar episodes is common, and symptoms may be duplicated by having the patient cough on request. The cause may be a decrease in cerebral blood volume due to the pronounced increase in intracranial pressure during a cough paroxysm.[47] A role of cerebral vascular disease affecting the carotid sinus has also been suggested.[48]

Micturition

Micturition syncope is observed almost exclusively in men, probably because of the standing position for urination. Symptoms may occur immediately before, during or after micturition. Episodes nearly always occur at night and may be secondary to orthostatic hypotension following the prolonged recumbency of sleep, plus vagal induced bradycardia.[49]

Glossopharyngeal Neuralgia

This is a syndrome of intermittent agonizing paroxysmal pain, localized to the tonsilar pillar or, occasionally, the external auditory meatus. It has been associated with syncope felt to be secondary to activation of glossopharyngeal-vagal reflex arc.[50] Atropine and Dilantin have been used to treat syncope in this condition but carbamazepine (Tegretol®), 400 to 1,000 mg every day, is clearly the drug of choice for the entire syndrome.[51]

Hysteria

Hysteria is a diagnosis of exclusion and is overdiagnosed. Suggestive features are lack of prodrome, possible secondary gain, bizarre postures and movements, lack of pallor and prolonged unconsciousness. Generally, the patient is young or has a well-documented history of hysterical reaction to stress. Without such history, the diagnosis of hysteria after the midtwenties is suspect.

During episodes of hysterical unconsciousness, ice-water irrigation against the tympanic membrane (30 ml of water with the patient's head at 30°) will produce brisk nystagmus with the fast component to the opposite side. If the patient is unconscious because of an organic cause the eyes will remain tonically deviated to the side of the irrigation.[52]

Narcolepsy

Males are affected by narcolepsy as often as females; the onset of the syndrome is most commonly between the second and third decades. Sleep attacks are often part of a syndrome characterized by a quartet as follows: (1) narcolepsy (sleep attacks)—one to multiple episodes or irresistible somnolence daily lasting minutes to several hours and producing a refreshing sleep; (2) cataplexy—sudden loss of postural muscle tone, usually preceded by an emotional stimulus (startle, laughing, fear, cough); (3) sleep paralysis —immobility of extremity muscles lasting seconds

during awakening or falling asleep; (4) hypnagogic hallucinations—vivid dreams, or nightmares, often occurring as the patient is falling asleep. One or any combination of the quartet may be found.[53] Antinarcoleptic treatment classically includes methylphenidate (Ritalin®) 40 to 80 mg every day, dextroamphetamine or ephedrine. Imipramine, 25 mg three times a day, is effective against cataplexy, sleep paralysis and hypnagogic hallucinations.[54]

Meniere's Disease

Meniere's disease is characterized by recurrent paroxysmal attacks of severe vertigo lasting up to several hours. Tinnitus and progressive hearing loss are found. Loss of consciousness of a few seconds is found in a small percentage of patients.[55] Basilar artery ischemic attacks pose a common differential diagnostic problem; scintillating scotomata accompanying the vertiginous attacks stamp the diagnosis as basilar artery ischemia. Dimenhydrinate (Dramamine®), 50 mg three times a day, is often helpful.

Swallow Syncope

This is a rare but potentially fatal form of syncope following swallowing. In most cases structural disease of the esophagus is felt responsible but cardiac and central nervous system lesions have been found. The attacks are aborted by atropine and the syndrome is felt to be vagally mediated.[56]

Summary

The differential diagnosis of episodic loss of consciousness has been presented. One should approach the problem by first considering simple faints or epilepsy. The various less common causes of a cardiovascular or cerebrovascular nature, as well as others, have been discussed here. It is important that these less commonly seen causes, which are often more serious, not be overlooked when diagnosing and treating transient loss of consciousness.

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